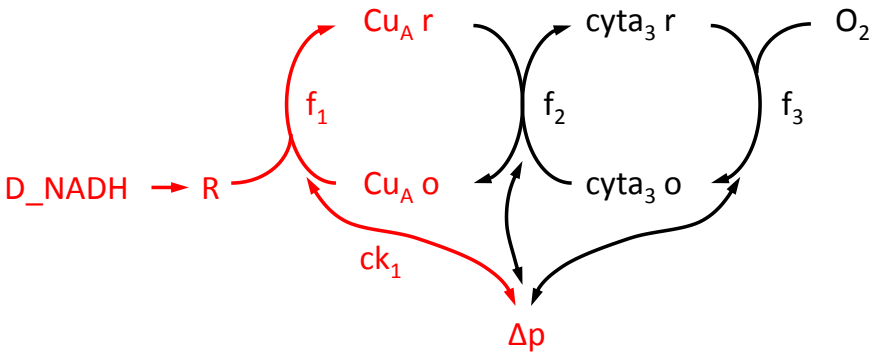

Supplement Fig. 2: Schematic representation of the mitochondrial submodel of the BRAINSIGNALS model. Highlighted in red are the aspects of this submodel that we investigated for the purpose of this paper.
The Cu_A centre is reduced ('r') by some reducing substrate, termed R. It in turn passes its electrons onto $cyta_3$. Finally $cyta_3$ is oxidised ('o') by oxygen. All processes can in general produce a proton motive force, Δp, by the movement of electrons and/or protons across the inner mitochondrial membrane. As a result, they are also inhibited by Δp. The rates of the three processes – initial reduction of Cu_A, electron transfer to $cyta_3$ and final oxidation of $cyta_3$, are termed f_1, f_2 and f_3, respectively.
The rate of Cu_A reduction (f_1) is dependent on the NAD/NADH ratio (via the effect of the model parameter D_NADH on R) and the proton motive force (via the model parameter ck_1 that determines the sensitivity of f_1 to changes in Δp). Incorporating a specific change in D_NADH during functional activation can therefore affect the size and sign of the Δ[oxCCO] signal. Changing the parameter ck_1 will affect the extent to which the Cu_A reduction rate responds to the change in Δp induced by the change in demand during functional activation. Again, this can affect the size and sign of the Δ[oxCCO] signal.